



February 2020

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## **CORPORATE REVIEW**

# A New Paradigm for the Treatment of Immune-Mediated Diseases

Nasdaq: ALDX  
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# Our Mission and Value Proposition

**Developing Next-Generation Medicines to Improve the Lives of Patients with Immune-Mediated Diseases**



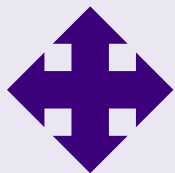
# Our Lead Programs Represent Compelling Commercial Opportunities

## Dry Eye Disease

### Reproxalap 0.25%



Early and consistent symptom and sign improvements in clinical trials\*



Broad symptom and sign improvements in clinical trials\*

**RENEW-Part 1 Phase 3  
Completed December 2019**

## Allergic Conjunctivitis

### Reproxalap 0.25%



Clinically significant and durable symptom response in allergen chamber trial



Active in post-histaminic allergy, for which no drug is approved

**INVIGORATE Phase 3  
Results H2 2020**

## Proliferative Vitreoretinopathy

### ADX-2191



Potential therapeutic breakthrough for PVR  
✓ U.S. orphan designation  
✓ FDA fast track designation



Reattachment success and tolerability demonstrated in Phase 1b clinical trial\*\*

**GUARD Phase 3 - Part 1  
Initiated December 2019**



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## **CORPORATE REVIEW**

# Ocular Disease Area

- **DRY EYE DISEASE**
- ALLERGIC CONJUNCTIVITIS
- PROLIFERATIVE VITREORETINOPATHY



# Reproxalap Represents a New Approach for Dry Eye Disease – A Persistently Disturbing And Inadequately Treated Condition

## Dry Eye Disease

**34**  
million

34 million or more adults in the U.S. suffer from DED.



Current Rx options may require up to six weeks or longer to achieve even modest efficacy.

Age 50+  
**>3x**

DED increases with age, with those over age 50 three times more likely to suffer from DED.

Up to  
**75%**

Up to 75% of patients with DED are not satisfied with current prescription options.



Women are twice as likely to suffer from DED than men.

Up to  
**80%**

Between 50% and 80% of Rx treated DED patients drop off of therapy between their second and third refill.



Significant negative quality of life impact

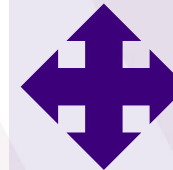
**Underserved Patient Population**

## Reproxalap

### Reproxalap in DED



Rapid and consistent symptom and sign improvements in clinical trials\*



Broad symptom and sign improvements in clinical trials\*

Subsequent development plans are contingent on FDA feedback in H1 2020

# Reproxalap's Novel Mechanism of Action Has The Potential to Provide Differentiated Activity Versus Existing Treatments

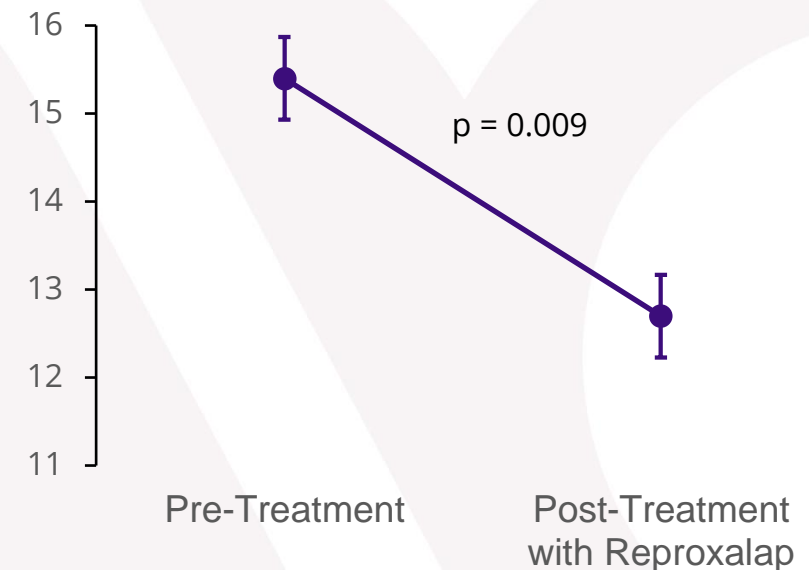
## RASP in Dry Eye Disease

- RASP markers are upregulated in patients with dry eye disease.
- RASP accumulation leads to changes in tear film and triggers an inflammatory response that can lead to acute and chronic inflammation.
- RASP levels correlate with worsening of dry eye disease symptoms and signs.
- **To our knowledge, reproxalap is the first dry eye disease drug to show biomarker changes correlated with clinical efficacy.**

## Reproxalap

- In a Phase 2a clinical trial, **reproxalap significantly reduced RASP adduct levels.**

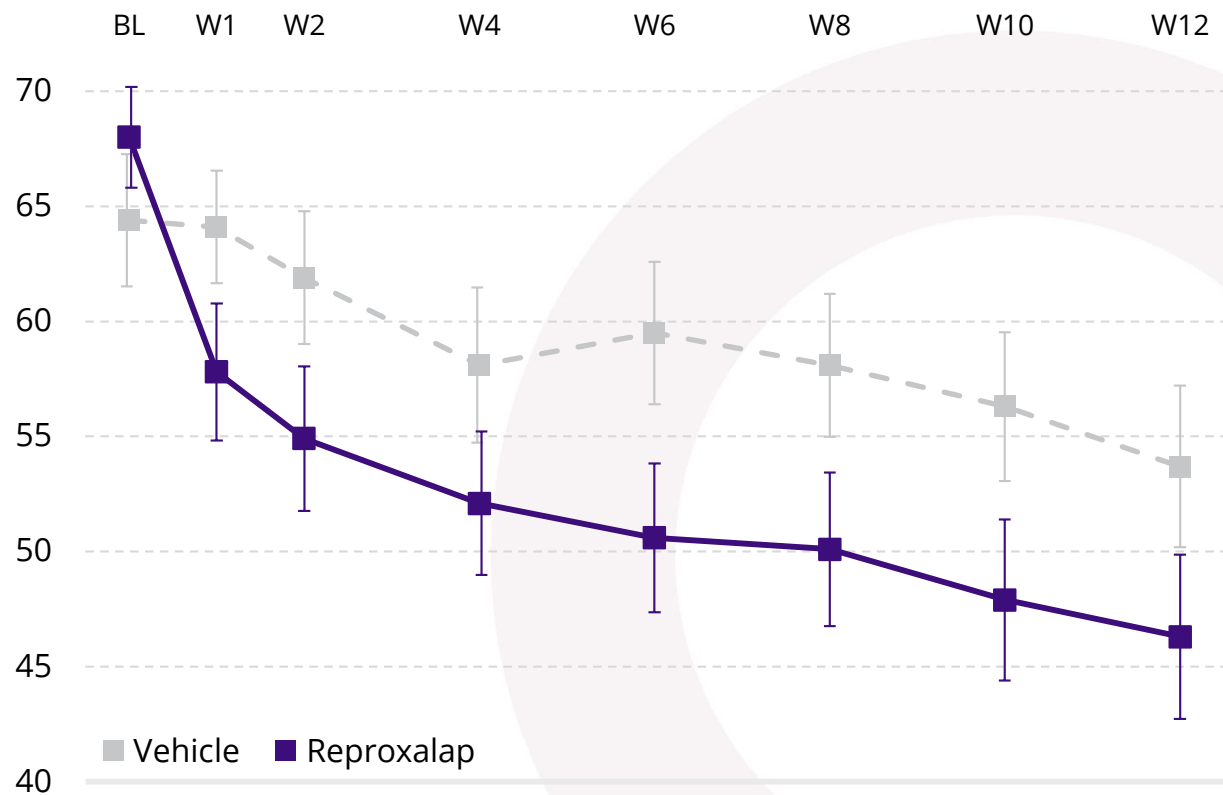
**Tear RASP Levels in Dry Eye Disease Patients**  
( $\mu\text{M}$  Malondialdehyde Adduct; Mean  $\pm$  Within-Subject SEM)



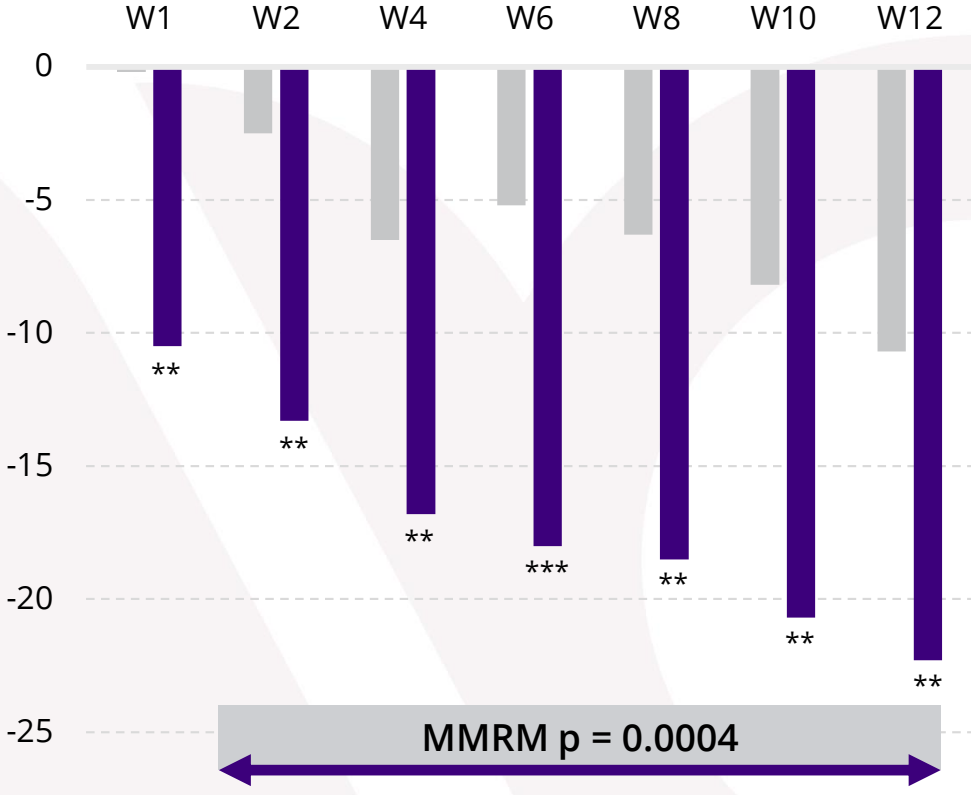
# Reproxalap Demonstrated Rapid and Durable Improvement in Co-Primary Endpoint of Ocular Dryness Score in RENEW-Part 1

## Co-Primary Symptom Endpoint for RENEW

Ocular Dryness Score (VAS)<sup>†</sup>  
Baseline and Weeks 1 to 12; ± Standard Error of the Mean



Ocular Dryness Score (VAS)<sup>†</sup> Change From Baseline  
Weeks 1 to 12



MMRM p = 0.0004

\*\*p<0.01 \*\*\*p<0.001

VAS = Visual Analog Scale

BL = Baseline; W = Week

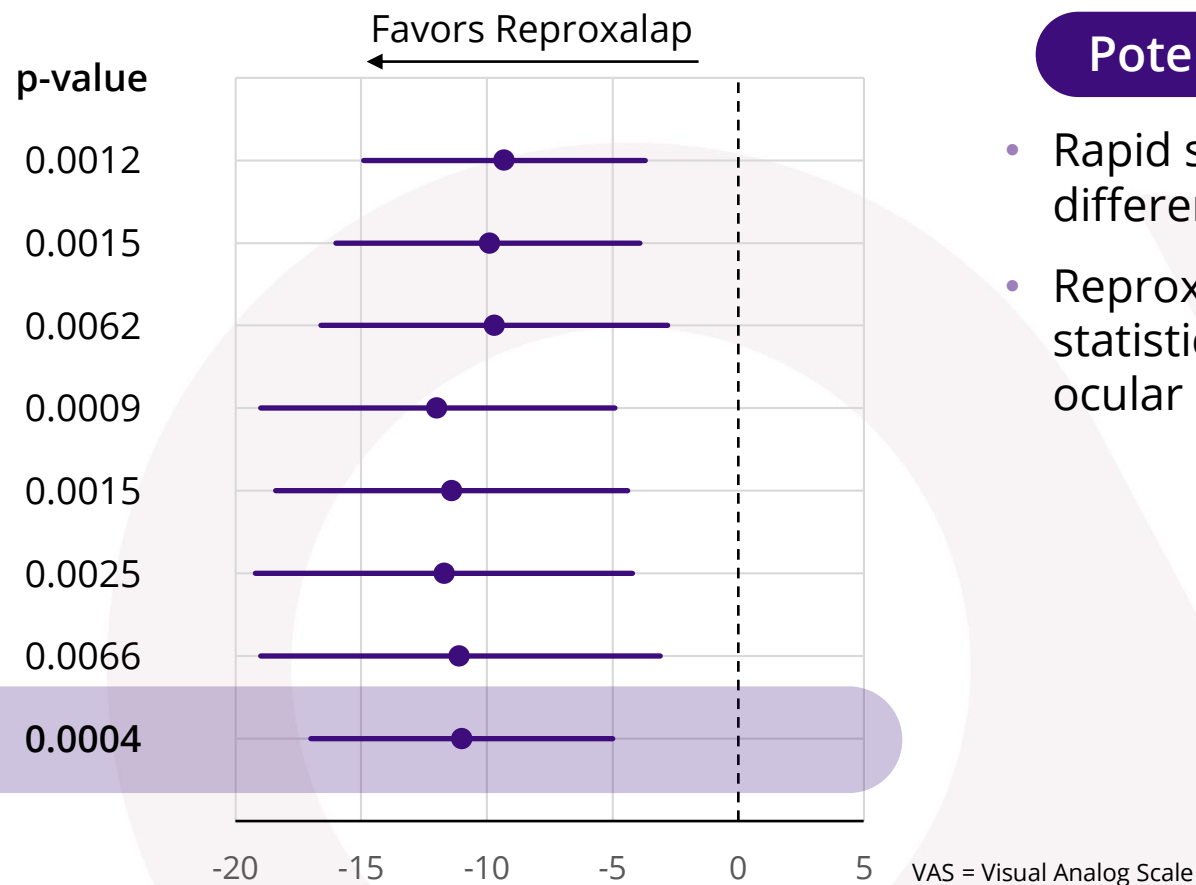
MMRM = Mixed Effect Model Repeated Measures

<sup>†</sup>Ocular Dryness Score co-primary endpoint assessed in pre-specified patient population having an ocular dryness (Ocular Dryness 4-Symptom) baseline score of ≥ 3 (N=170). Topical ocular reproxalap has been studied in over 1,100 patients with no observed safety concerns; mild instillation site irritation is the most commonly reported adverse event in clinical trials.  
Source: RENEW-Part 1 induction-maintenance top-line results



# Reproxalap Demonstrated Highly Statistically Significant Reductions in Ocular Dryness in RENEW-Part 1

## Ocular Dryness Score (VAS) Treatment Difference (Reproxalap-Vehicle)\*



### Potential Competitive Advantages<sup>†</sup>

- Rapid symptom improvement supports differentiated product profile.
- Reproxalap demonstrated large and statistically significant improvements in ocular dryness at every time point.

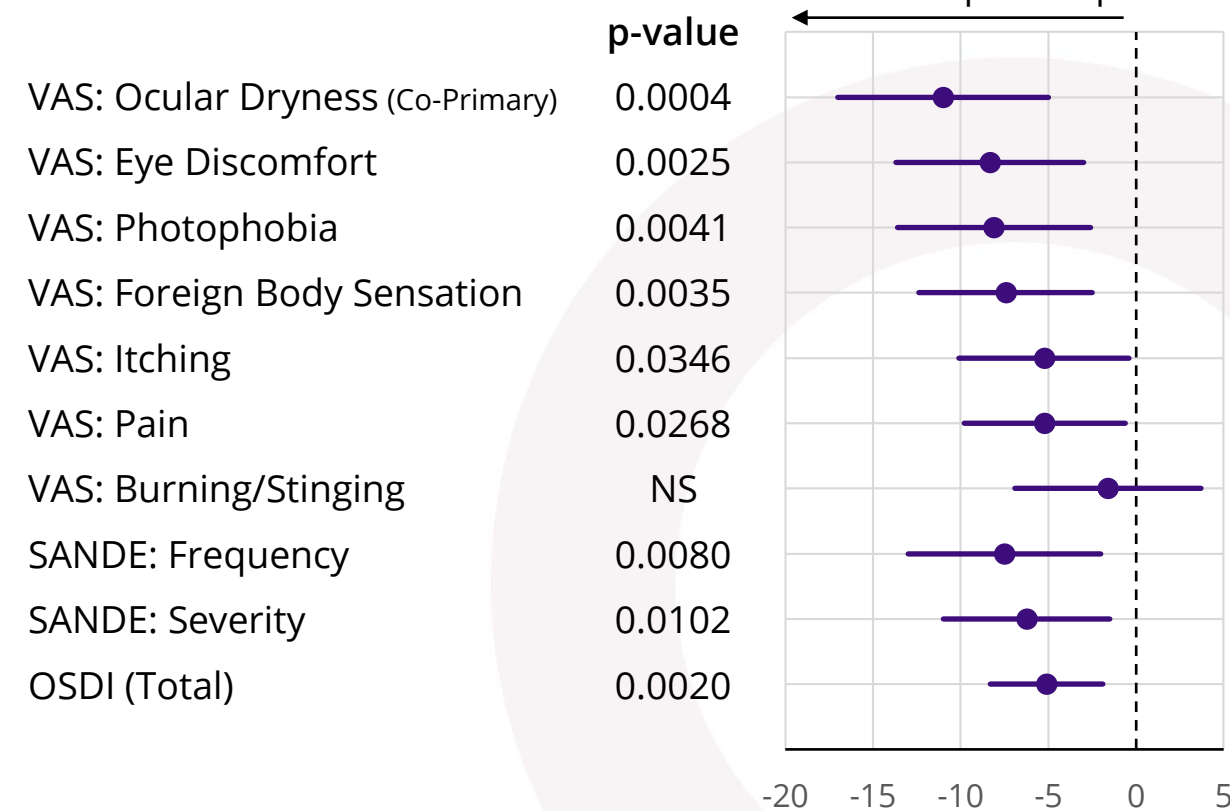
<sup>†</sup>Pending clinical data, regulatory discussions, payor negotiations, competition, potential legislative changes, and other factors, which may not be in Aldehyra's control.

\*Treatment Difference defined as the difference between the changes from baseline for the evaluated drug vs. vehicle (LS Mean Difference  $\pm$  95% CI). Topical ocular reproxalap has been studied in over 1,100 patients with no observed safety concerns; mild instillation site irritation is the most commonly reported adverse event in clinical trials. Ocular Dryness Score co-primary endpoint assessed in pre-specified patient population having an OD4S dryness baseline score of  $\geq 3$  (N=170).  
Source: RENEW-Part 1 induction-maintenance top-line results

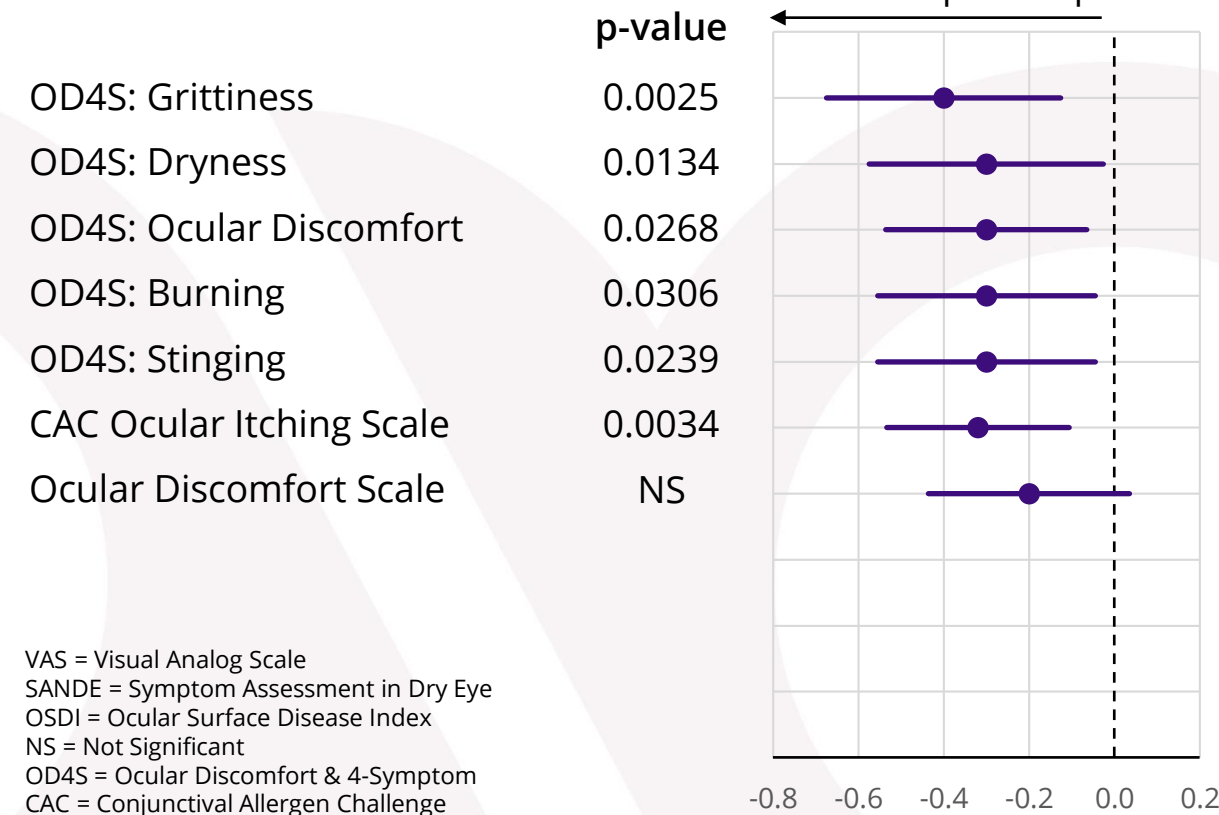
# Reproxalap Demonstrated Broad Statistically Significant Symptom Improvement in RENEW-Part 1

## Symptom Treatment Difference\* (Reproxalap-Vehicle) Over Weeks 2 to 12

### 0-100 Ocular Symptom Scales



### 0-4 & 0-5 Ocular Symptom Scales

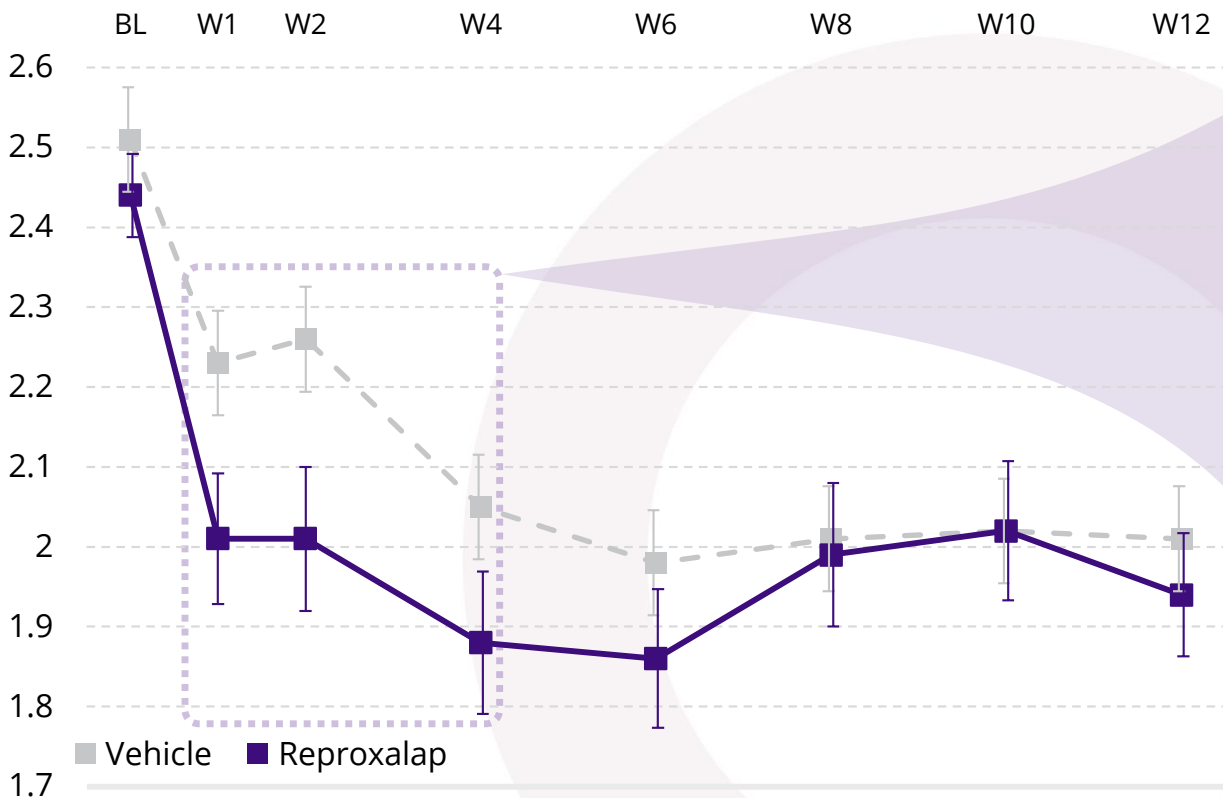


VAS = Visual Analog Scale  
 SANDE = Symptom Assessment in Dry Eye  
 OSDI = Ocular Surface Disease Index  
 NS = Not Significant  
 OD4S = Ocular Discomfort & 4-Symptom  
 CAC = Conjunctival Allergen Challenge

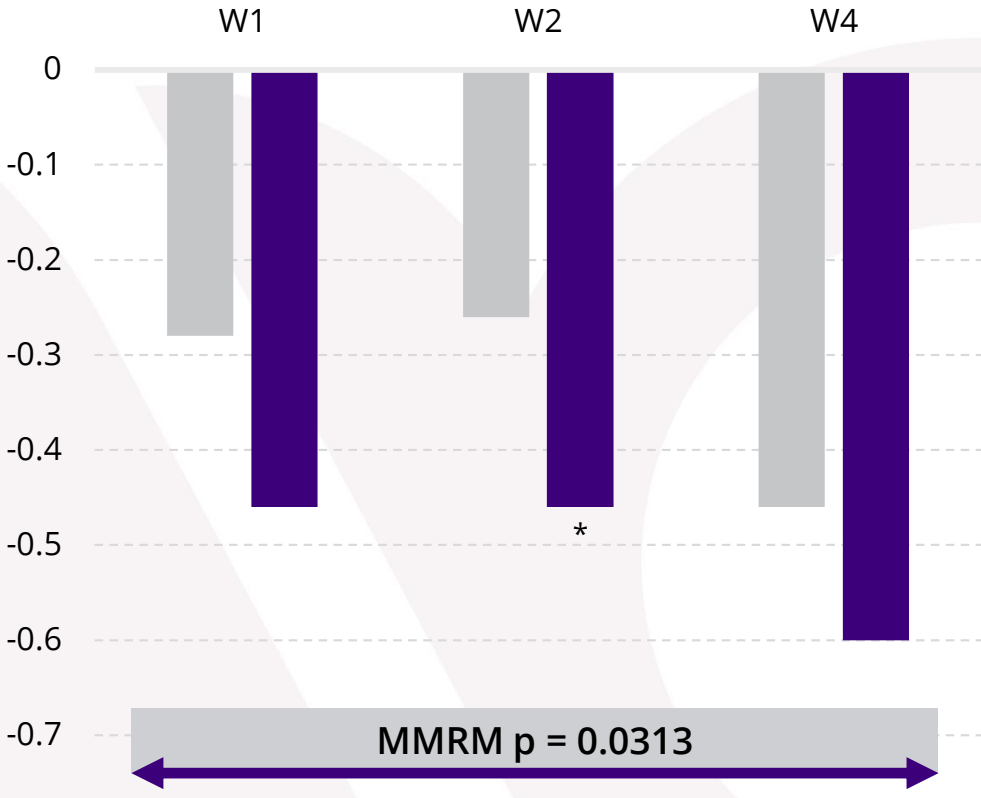
# Reproxalap Demonstrated Rapid Improvement in Co-Primary Endpoint of Fluorescein Staining Score in RENEW-Part 1

## Co-Primary Sign Endpoint for RENEW

Fluorescein Staining: Nasal Region† (0-4)  
Baseline and Weeks 1 to 12; ± Standard Error of the Mean



Fluorescein Staining: Nasal Region† Change From Baseline  
Weeks 1 to 4



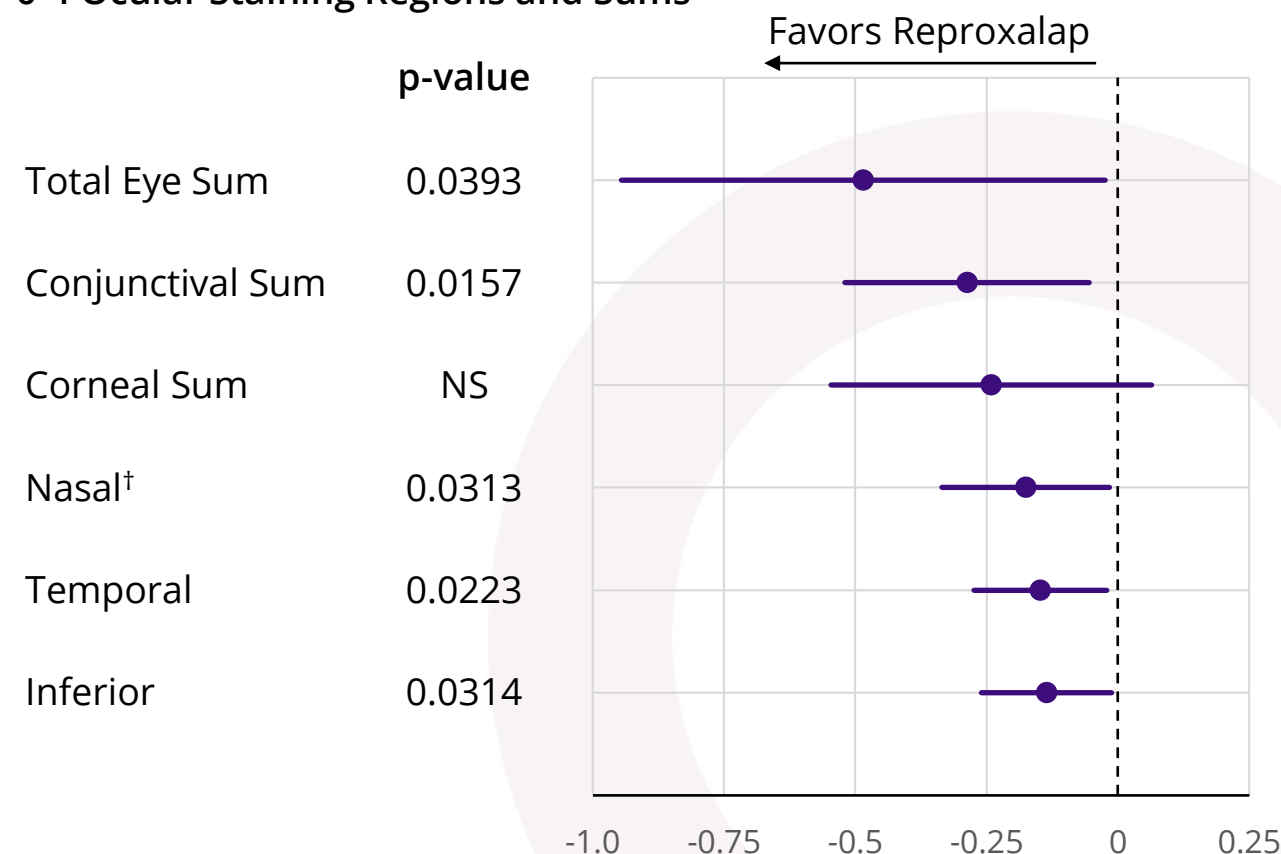
†Fluorescein Staining co-primary endpoint assessed in pre-specified patient population having a nasal region baseline score of  $\geq 2$  (N=179). Topical ocular reproxalap has been studied in over 1,100 patients with no observed safety concerns; mild instillation site irritation is the most commonly reported adverse event in clinical trials.  
Source: RENEW-Part 1 induction-maintenance top-line results

\*p<0.05  
BL = Baseline; W = Week  
MMRM = Mixed Effect Model Repeated Measures (across 12 weeks)

# Reproxalap Demonstrated Rapid and Broad Staining Improvements in RENEW-Part 1

## Fluorescein Staining Treatment Difference (Reproxalap-Vehicle) Over Weeks 1 to 4\*

### 0-4 Ocular Staining Regions and Sums



### Potential Competitive Advantages†

- Rapid sign improvement supports differentiated product profile.
- Reproxalap demonstrated statistically significant improvements over vehicle in majority of regions over Weeks 1 to 4.
- Reproxalap demonstrated substantial improvements at Week 1, with near-peak difference from vehicle achieved by Week 4.

Total Eye Sum = All five regions  
Conjunctival Sum = Nasal + Temporal  
Corneal Sum = Inferior + Central + Superior

†Pending clinical data, regulatory discussions, payor negotiations, competition, potential legislative changes, and other factors, which may not be in Aldeyra's control.

\*Treatment Difference defined as the difference between the changes from baseline for the evaluated drug vs. vehicle (LS Mean Difference  $\pm$  95% CI). Topical ocular reproxalap has been studied in over 1,100 patients with no observed safety concerns; mild instillation site irritation is the most commonly reported adverse event in clinical trials.

†Fluorescein Staining co-primary endpoint assessed in pre-specified patient population having a nasal region baseline score of  $\geq 2$  (N=179).

Source: RENEW-Part 1 induction-maintenance top-line results



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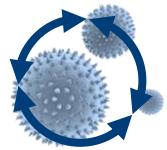
## **CORPORATE REVIEW**

# Ocular Disease Area

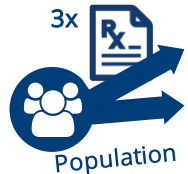
- DRY EYE DISEASE
- **ALLERGIC CONJUNCTIVITIS**
- PROLIFERATIVE VITREORETINOPATHY

# Reproxalap Represents a New Approach for Allergic Conjunctivitis – A Burdensome and Growing Disease with Unmet Medical Need

## Allergic Conjunctivitis



Allergy seasons are getting **longer and more severe** with pollen spreading to new areas.



AC prescription volume is growing **3x faster** than the U.S. population.\*



Up to 30 million of AC sufferers in the U.S. **do not respond** adequately to or are dissatisfied with antihistamines.



Many AC patients make **significant sacrifices** due to lack of drug activity.



Antihistamines are not **effective** in an estimated 24% of treated AC patients.†



Nearly 1 in 4 of AC patients are using corticosteroid and/or NSAID eye drops\*\*.



**Growing and burdensome** unmet medical need

**Underserved Patient Population**

## Reproxalap

### Reproxalap in AC



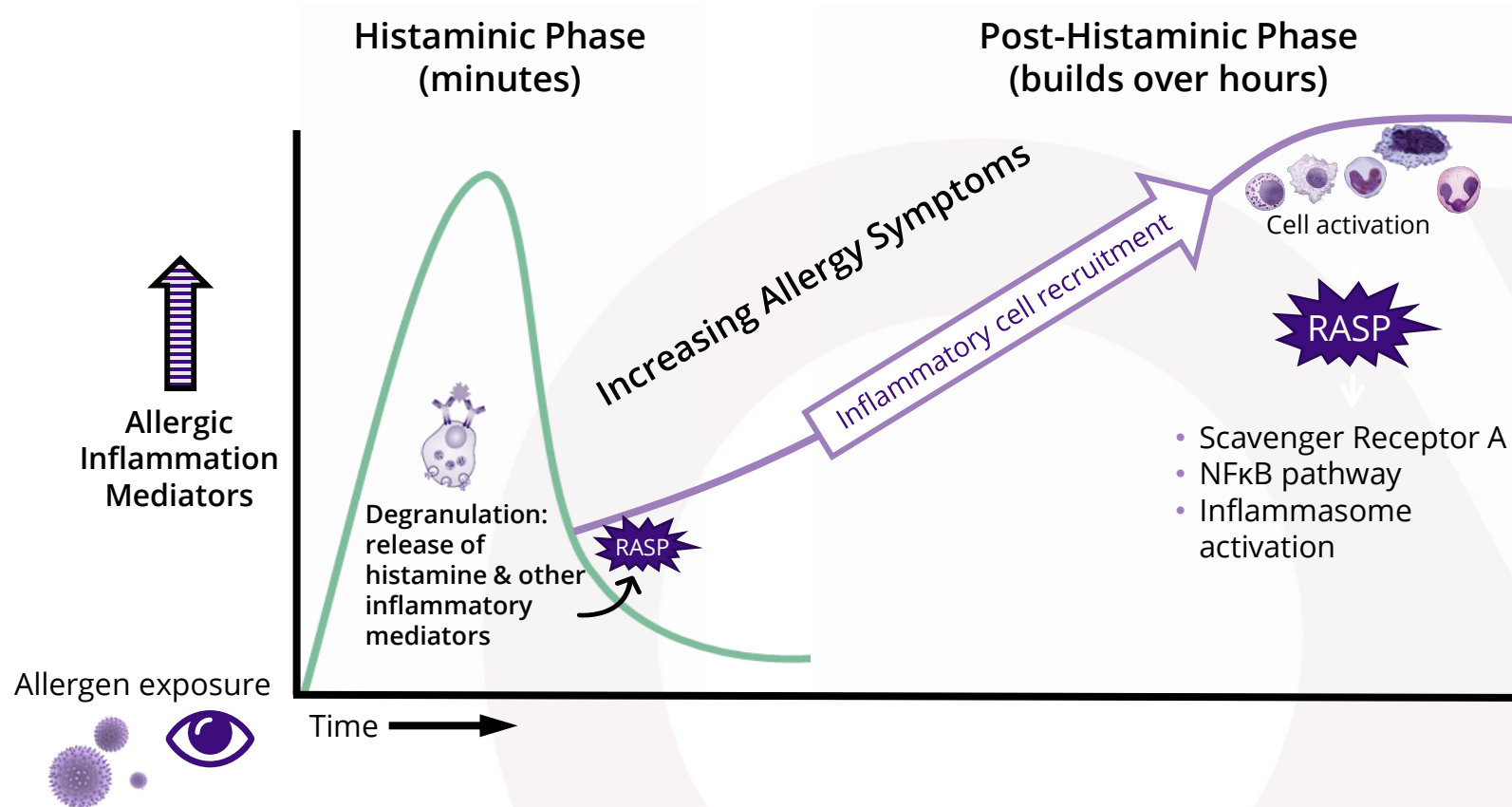
Clinically significant and durable symptom response in ALLEVIATE Phase 3 and allergen chamber clinical trials



Active in post-histaminic allergy, for which no drug is approved



# Reproxalap's Novel Mechanism of Action Has The Potential to Provide Differentiated Activity Versus Antihistamines

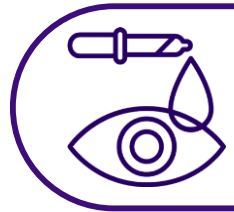


## Reproxalap

- Reproxalap irreversibly inhibits RASP, limiting allergic inflammation.
- Reproxalap has the potential to provide differentiated activity in post-histaminic allergy, which affects all allergic conjunctivitis patients.

# Reproxalap Has The Potential to be the First Novel Allergic Conjunctivitis New Drug Application in Decades

## Reproxalap's Phase 3 Program Utilizes Two Allergic Conjunctivitis Clinical Models



### Conjunctival Allergen Challenge

*Investigator administers one drop of allergen mixture on to the eye and records results.*

60 minutes post allergen exposure evaluated

### ALLEVIATE

Positive Results Announced March 2019



### Allergen Chamber

*Investigator monitors and assists patients in a controlled allergen chamber.*

3.5 hours of continuous allergen exposure evaluated

### INVIGORATE

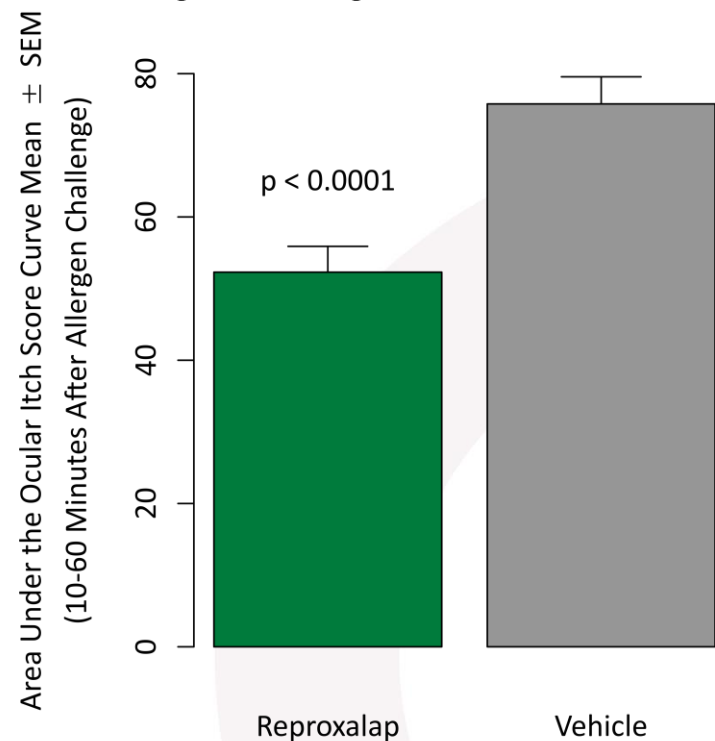
Initiated January 2020

- ✓ Supported by positive allergen chamber trial results

# Reproxalap Demonstrated Greater and More Durable Clinical Responses than Vehicle Group in ALLEVIATE Phase 3 Clinical Trial

## Primary Endpoint

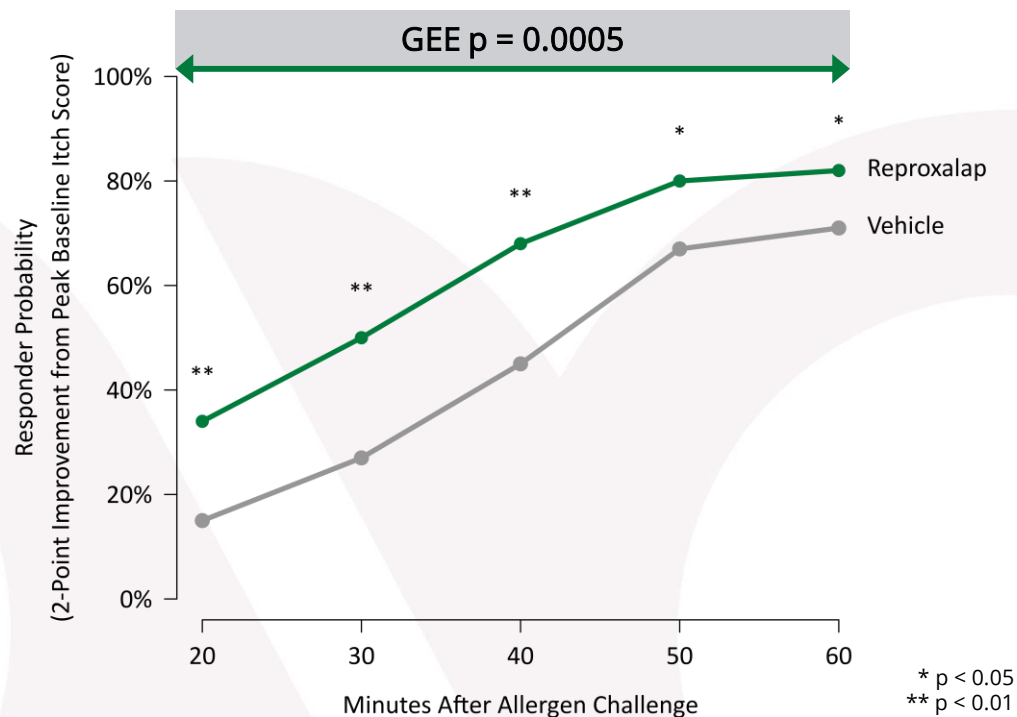
Area Under the Curve: Ocular Itch Score (0-4) 10 to 60 Minutes After Conjunctival Allergen Challenge



Improvement in itch score over one hour after allergen exposure statistically greater for reproxalap vs. vehicle

## Key Secondary Endpoint

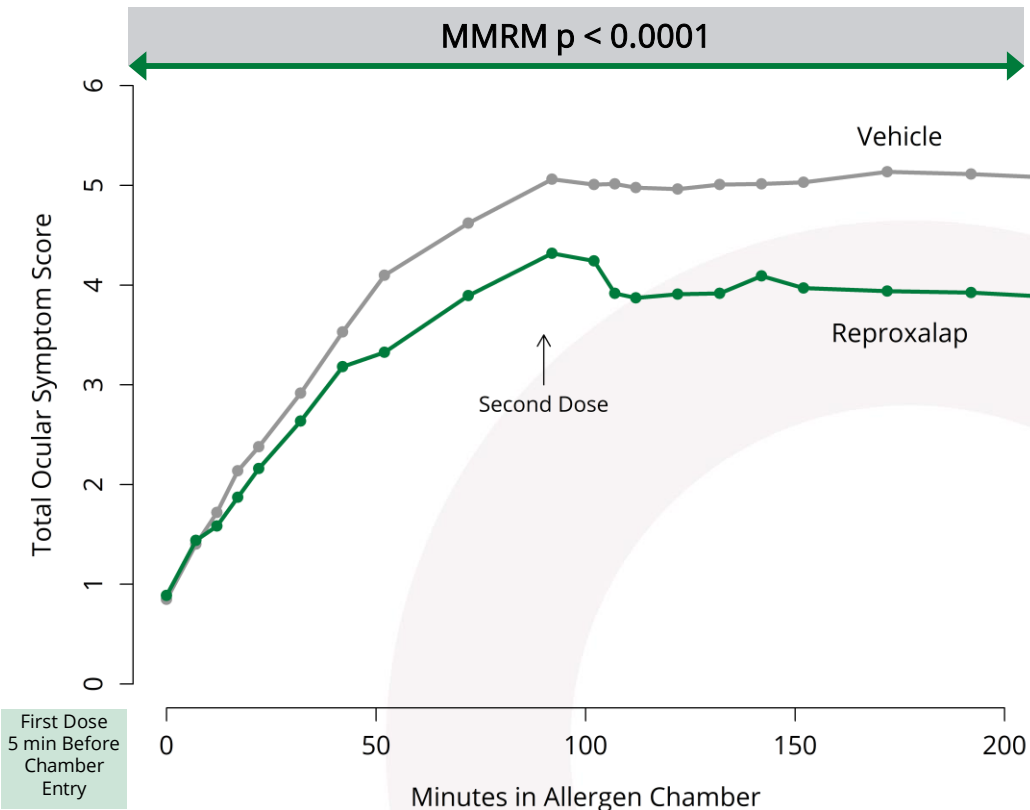
Probability of Two-Point Response: Ocular Itch Score (0-4) 20 to 60 Minutes After Conjunctival Allergen Challenge



Clinically significant response rate of reproxalap statistically higher than that of vehicle

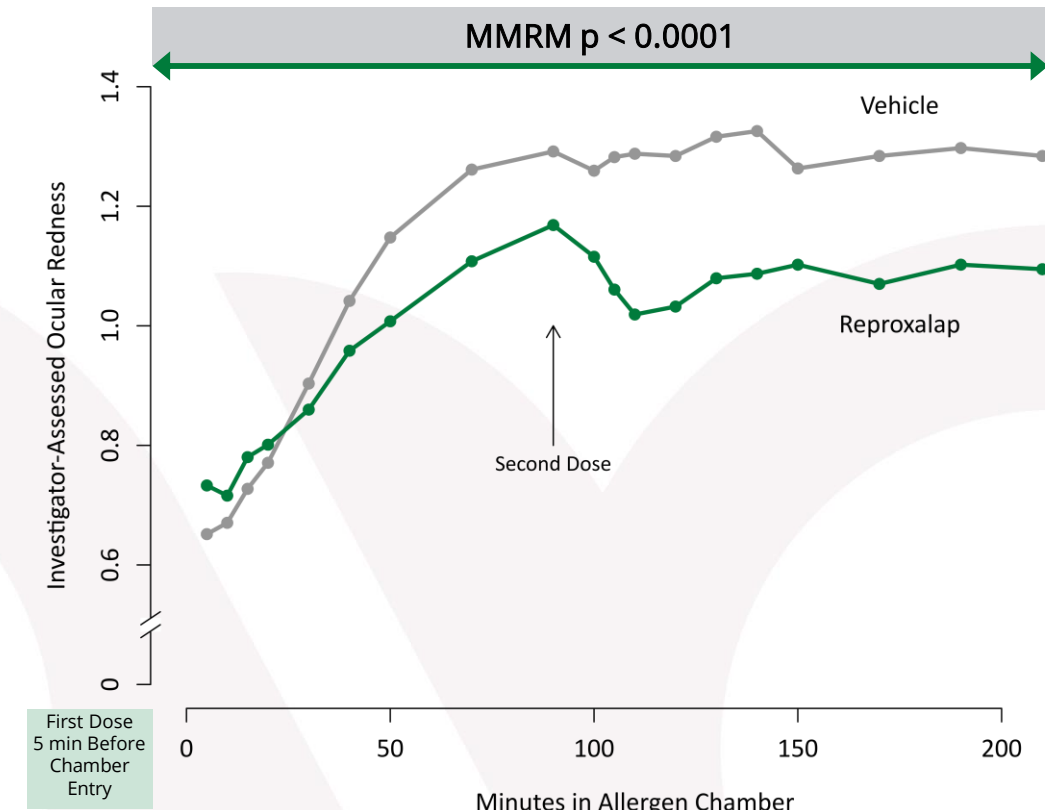
# Reproxalap Demonstrated Greater and More Durable Clinical Responses than Vehicle in Allergen Chamber Clinical Trial

Total Ocular Symptom Score (0-11 scale) During 3.5 Hours of Exposure



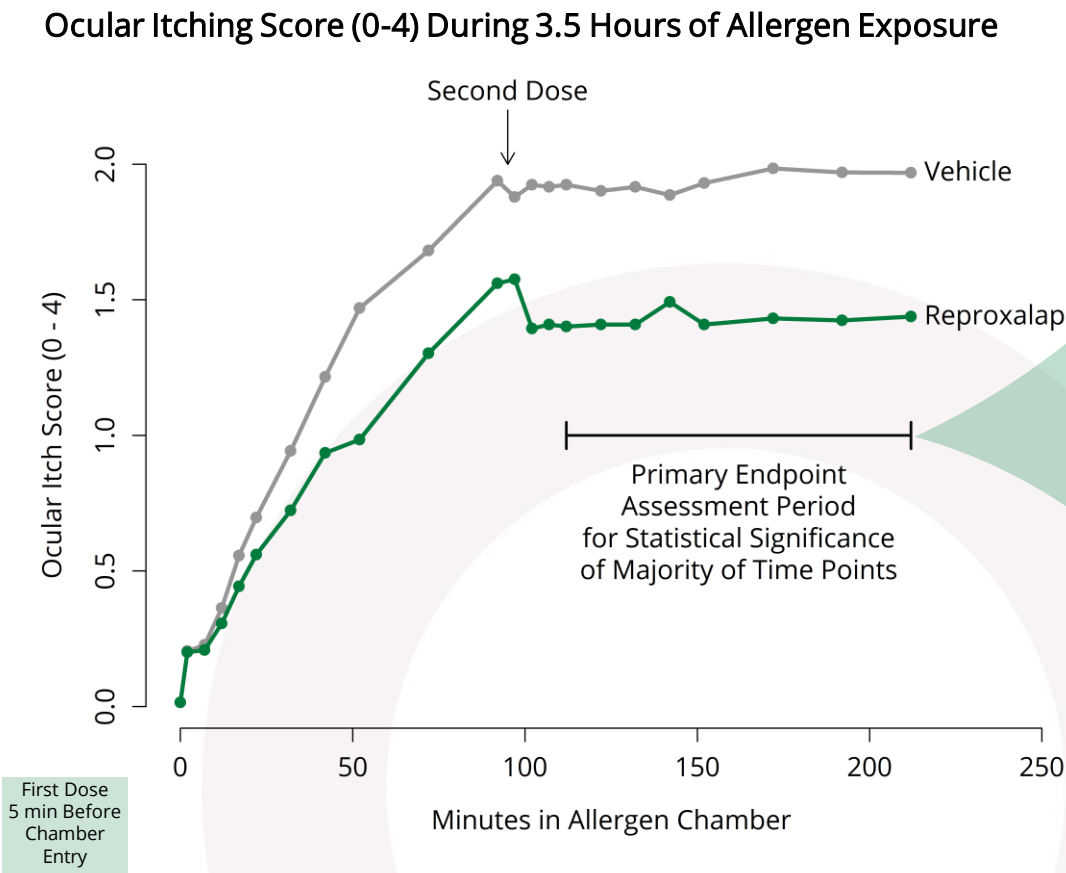
Statistically significant reduction in all assessed ocular symptoms and signs (itch, redness, and tearing) for 3.5 hours of continuous exposure to allergen

Ocular Redness Score (0-4) During 3.5 Hours of Exposure



Statistically significant reduction in ocular redness vs. vehicle for 3.5 hours of continuous exposure to allergen

# Confirmed INVIGORATE Phase 3 Primary Endpoint Achieved in Allergen Chamber Clinical Trial\*



Allergen chamber time point	p value
112	0.0002
122	0.0004
132	0.0002
142	0.0044
152	0.0001
172	<0.0001
192	<0.0001
212	0.0002

All time points from 110 to 210 minutes were statistically significant in Allergen Chamber trial



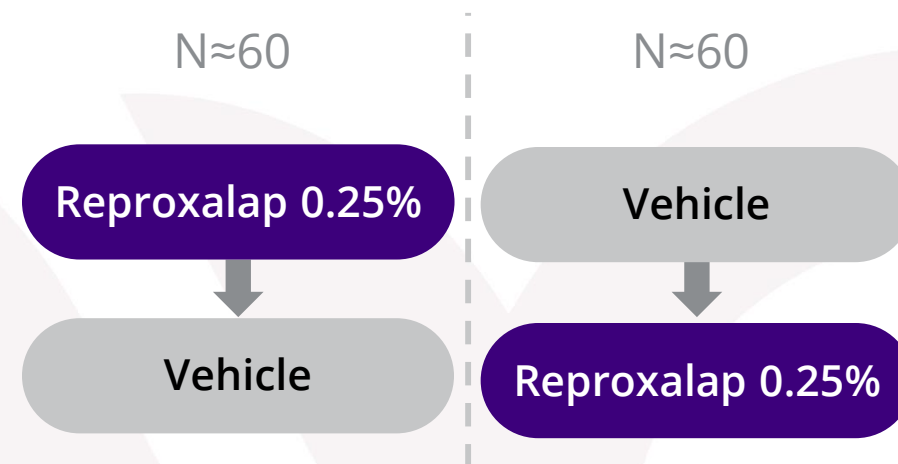
\*The safety and efficacy results of later phase or subsequent clinical trials may not confirm the results of earlier trials; p-value derived from Mixed effect Model Repeat Measurement (MMRM) time point analyses. Topical ocular reproxalap has been studied in over 1,100 patients with no observed safety concerns; mild instillation site irritation is the most commonly reported adverse event in clinical trials.

Source: Aldeyra Therapeutics allergen chamber clinical trial – reproxalap 0.25% (ClinicalTrials.gov #NCT03709121); n=66

# The INVIGORATE Phase 3 Clinical Trial Design

- **Primary endpoint:**
  - Statistical significance in ocular itch (0-4 scale) at a majority of eleven time points between 110 and 210 minutes
- **Secondary endpoints:**
  - Investigator-assessed ocular redness score
  - Patient-reported ocular tearing score
  - Total ocular symptom score
- **Inclusion/exclusion criteria:**
  - History of moderate to severe allergic conjunctivitis to ragweed pollen
  - Itching score of  $\geq 2.5$  or redness score  $\geq 2$  in baseline chamber test
- **Chamber exposure and dosing schedule:**
  - 3.5 hours continuous allergen exposure
  - First dose 5 minutes before chamber entry
  - Second dose 90 minutes after entry (when non-treated patients reach peak allergy symptoms)

## Two-Way Randomized Crossover



Results Expected H2 2020





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## **CORPORATE REVIEW**

# Ocular Disease Area

- DRY EYE DISEASE
- ALLERGIC CONJUNCTIVITIS
- **PROLIFERATIVE VITREORETINOPATHY**

# ADX-2191 Represents a New Approach for PVR

## – A Rare Sight-Threatening Retinal Disease With No Approved Therapy

### Proliferative vitreoretinopathy

### ADX-2191

4,000  
U.S.

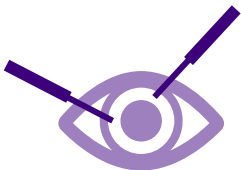
PVR is a **rare disease**, with ~4,000 patients per year in the U.S. and nearly twice as many in Europe and Japan combined.



Left untreated, retinal detachment due to PVR can progress to **permanent blindness**.



There is currently **No FDA- or EMA-approved therapy**.



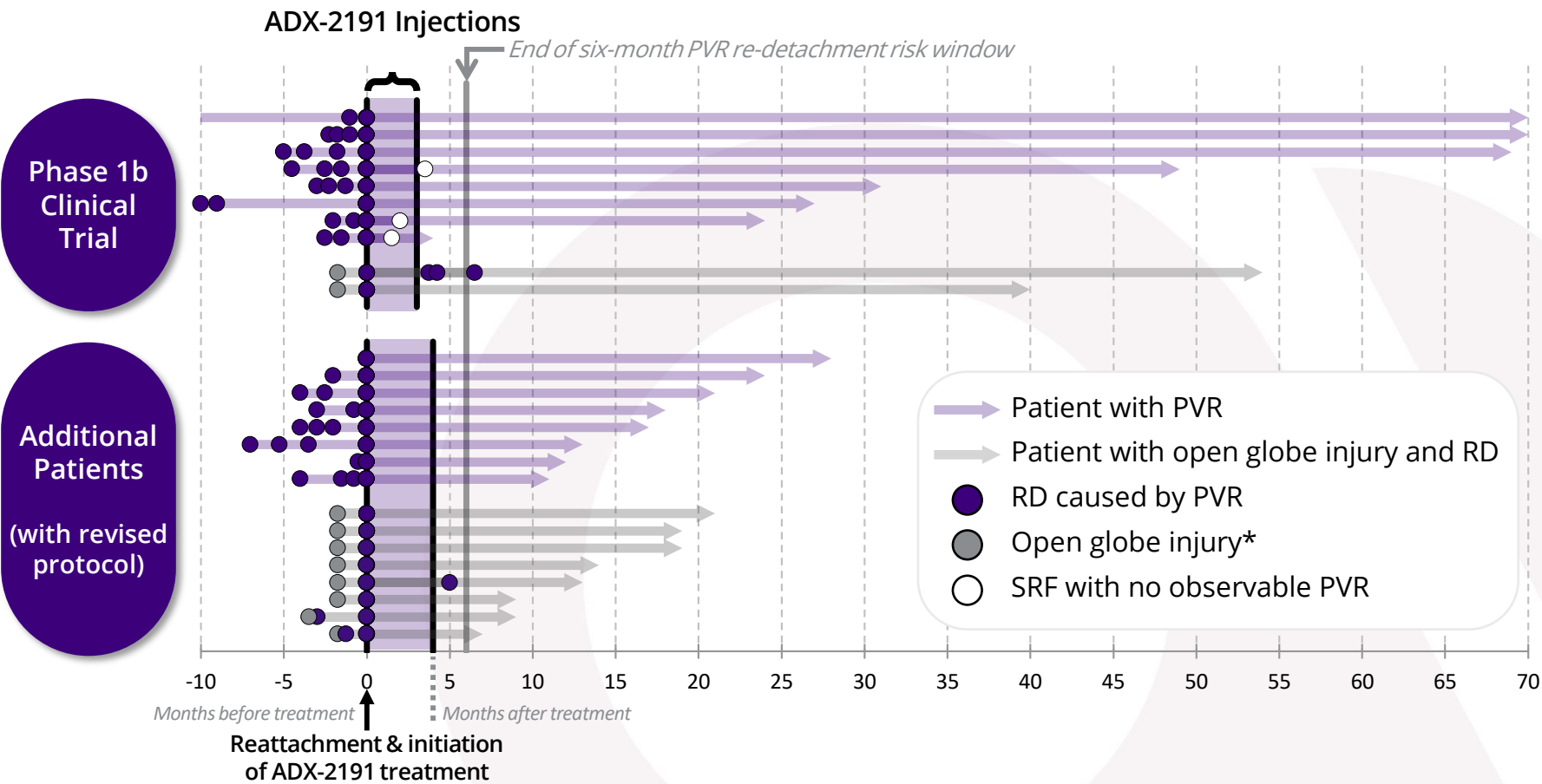
**Repeat surgery**, which can lead to **vision loss**, is currently the only possible course of action.

### ADX-2191

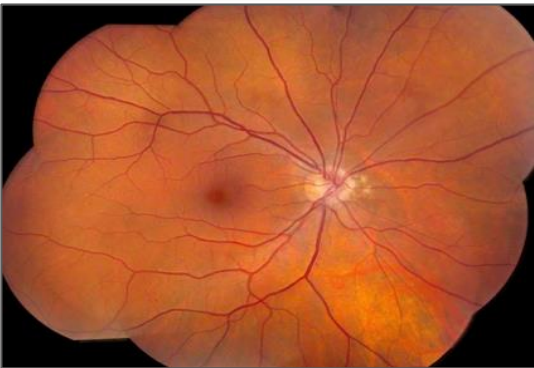
- A **novel approach and potential therapeutic breakthrough** in PVR treatment
- **Granted U.S. orphan designation** for the prevention of PVR
- **Granted FDA fast track designation** for the prevention of PVR
- **Tolerability and reattachment success** during study period **demonstrated in Phase 1b** open-label investigator sponsored clinical trial
- **GUARD adaptive Phase 3 clinical trial initiated December 2019**

# ADX-2191 Reduced Recurrent Retinal Detachment in Investigator Sponsored Phase 1b Clinical Trial and in Additional In-Practice Use

Retinal Detachments Over Time by Patient



Normal Retina



Retinal Detachment Due to PVR



\*Timing of open globe injury as shown is estimated. Typically 6-8 weeks prior to reattachment & initiation of ADX-2191. There is no assurance that prior results, such as signals of safety, activity or durability of effect, observed from this open label investigator sponsored trial will be replicated in more rigorous clinical trials involving ADX-2191. Source: ADX-2191 PVR Phase 1b investigator sponsored clinical trial (n=10) results and additional in-practice use (n=16)

# ADX-2191: GUARD Trial Design in Proliferative Vitreoretinopathy

## Adaptive Phase 3 (Part 1) Clinical Trial Design

- **Primary objective:**

- Evaluate efficacy of intravitreal ADX-2191 injections for prevention of recurrent retinal detachment due to proliferative vitreoretinopathy (PVR)

- **Design:**

- Multi-center, randomized, controlled, two- part, adaptive Phase 3 clinical trial

- **Inclusion highlights:**

- Recurrent retinal detachment due to PVR, or
- Retinal detachment associated with open-globe injury

- **Dosing regimen:**

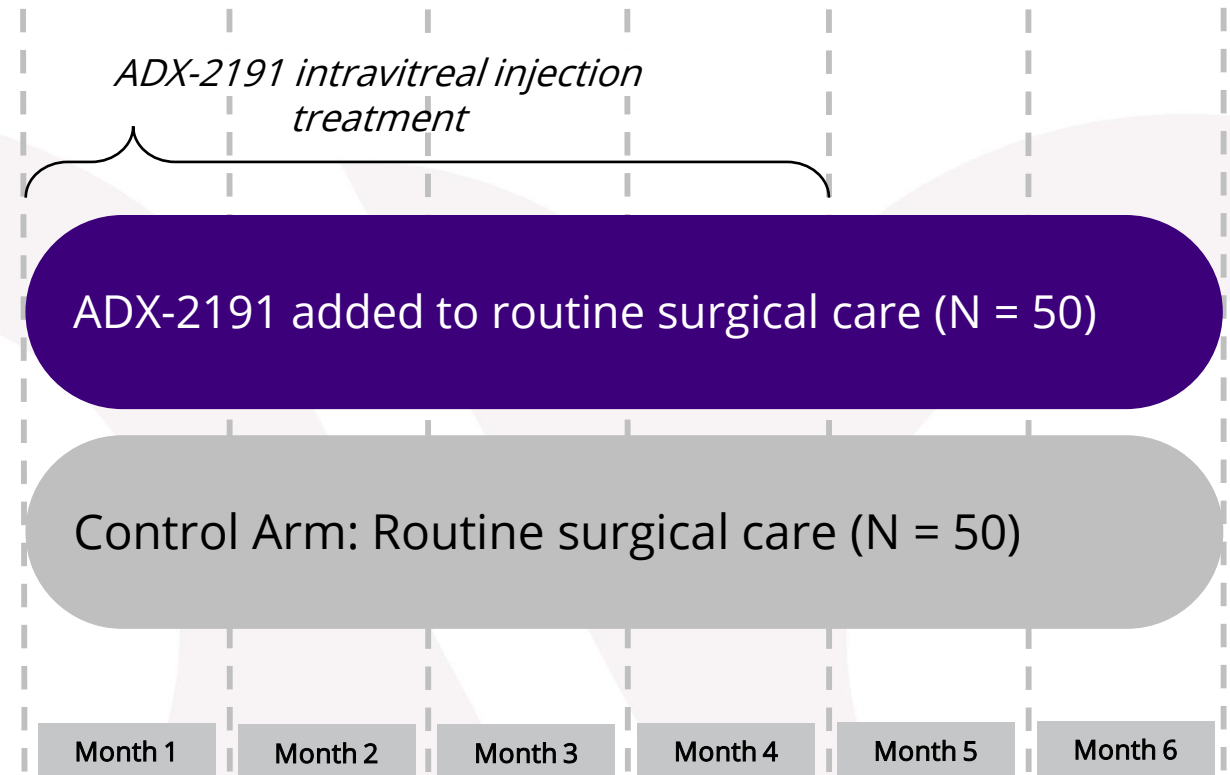
- At surgery, weekly (x8), and then every other week (x4) intravitreal ADX-2191 injections

- **Endpoint:**

- Retinal re-detachments due to PVR requiring re-operation within 6 months:
  1. OCT demonstrating fovea-off retinal detachment
  2. Photographic documentation retinal detachment

Initiated December 2019

### Adaptive Phase 3 PVR Clinical Trial Design: Part 1





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## **CORPORATE REVIEW**

# Systemic Disease Area

- SJÖGREN-LARSSON SYNDROME

# Reproxalap Represents a New Approach For SLS

## – A Rare RASP-Mediated Disease with No Approved Therapy

### Sjögren-Larsson Syndrome

1,000  
U.S.

SLS is a rare inborn error of metabolism caused by a mutation in the gene encoding fatty aldehyde dehydrogenase; there are ~1,000 SLS patients in the U.S. and a greater number in Europe.



Severe symptoms significantly impact SLS patient and caregiver quality of life.



There is currently no FDA- or EMA-approved therapy.



Nonstop disease burden diminishes quality of patient/caregiver life, with hours devoted to managing painful scaling, monitoring, & care.

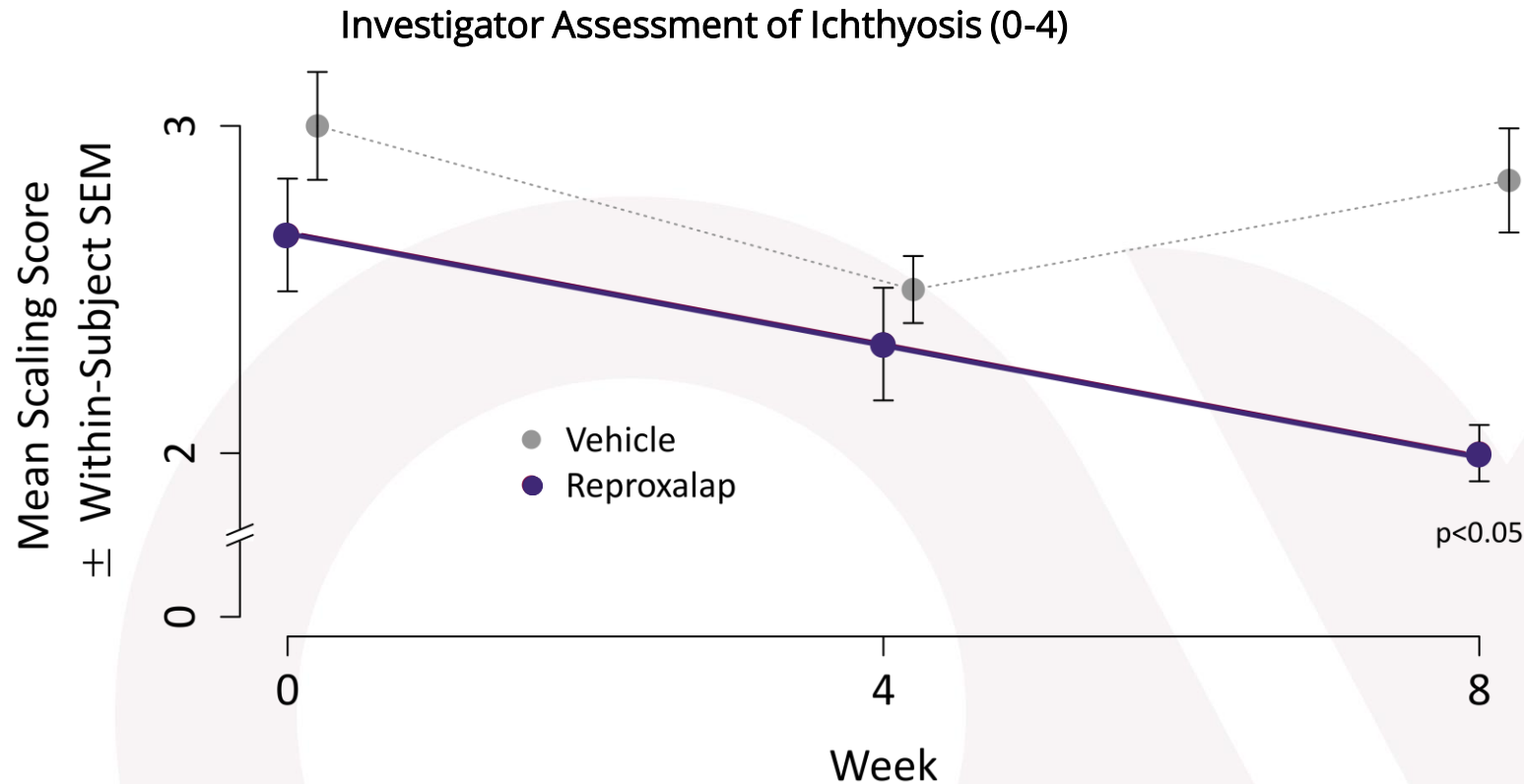
### Reproxalap

#### Reproxalap

- A novel approach and potential lifelong therapy to replace missing enzymatic activity in SLS
- Granted U.S. orphan designation for the treatment of congenital ichthyosis (primary symptom of SLS)
- Significantly reduced SLS ichthyosis in a randomized, vehicle-controlled Phase 2 clinical trial
- RESET Phase 3-Part 1 completed Q2 2019; results to be discussed with regulatory authorities prior to initiating subsequent clinical testing

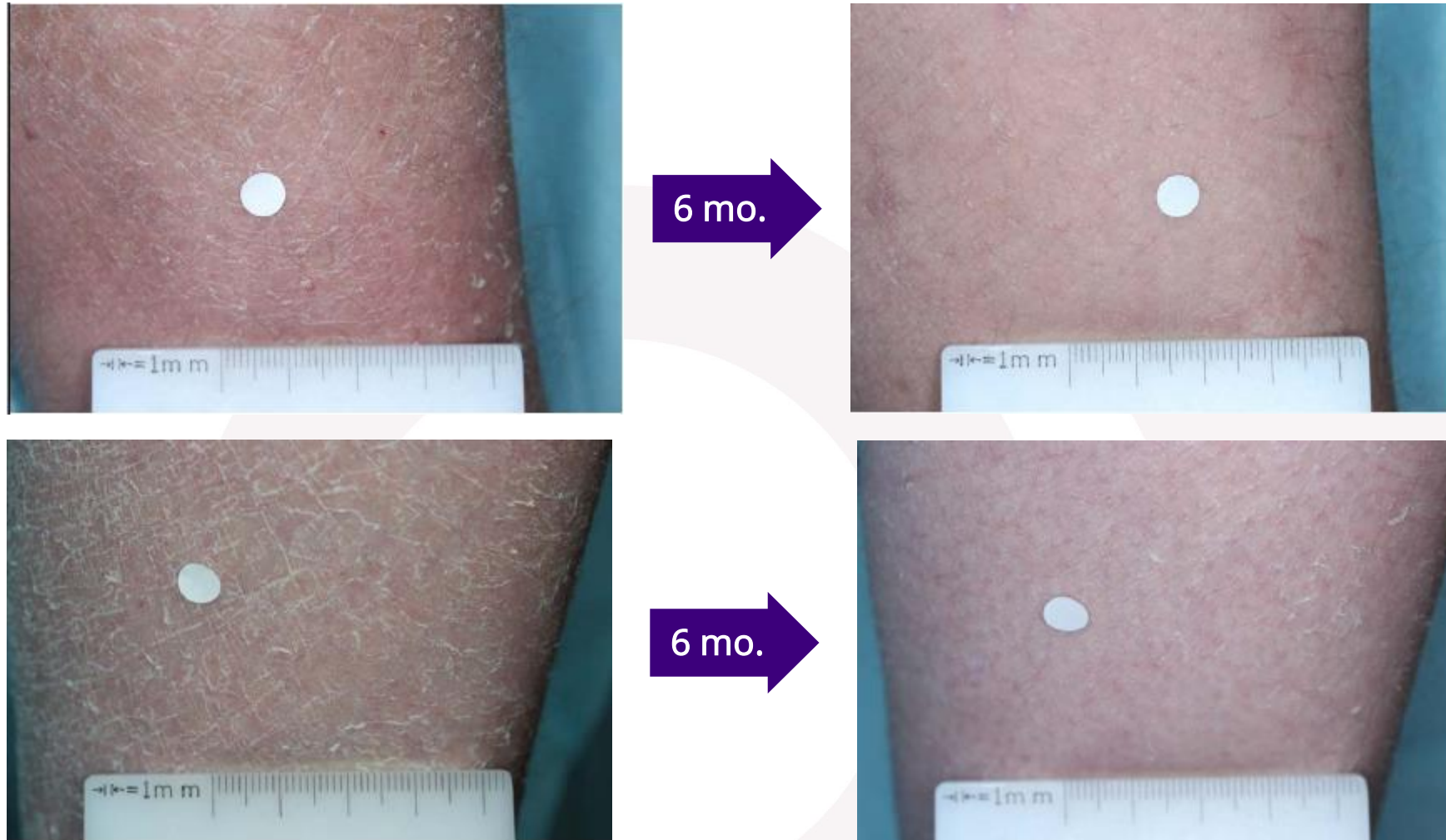


# Reproxalap Demonstrated Clinically Relevant and Consistent Activity in Phase 2 Clinical Trial



Over two months of treatment, ichthyosis improved consistently from moderate to mild disease

# Scaling Scores Statistically Lower Than Baseline Observed in Reproxalap-Treated Patients in RESET Part 1





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**CORPORATE REVIEW**

# An Innovative Platform for Ocular and Systemic Immune- Mediated Diseases

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# Deep and Innovative Pipeline Focused on Immune-Mediated Diseases

Disease Area	Compound	Mechanism	Indication	Preclinical	Phase 1	Phase 2	Phase 3
Ocular Diseases	Reproxalap	RASP	Dry Eye Disease				
			Allergic Conjunctivitis				
	ADX-2191	DHFR	Proliferative Vitreoretinopathy				
	ADX-103/10X	RASP	Retinal Disease				
	Undisclosed		Ocular Inflammation	Research Collaboration (undisclosed)			
Systemic Diseases	Reproxalap	RASP	Sjögren-Larsson Syndrome				
	ADX-1612	CHP	PTLD				
			Mesothelioma	Investigator-Sponsored Trial			
			Ovarian Cancer	Investigator-Sponsored Trial			
	ADX-629	RASP	Autoimmune / Metabolic Disease				
	ADX-1615	CHP	Autoimmune Disease / Cancer				
	Undisclosed	RASP	Systemic Inflammatory Disease				

# Experienced Management Team and Board of Directors

## Management Team

**Todd Brady, M.D., Ph.D.**  
President, CEO, & Director

**Joshua Reed, M.B.A.**  
Chief Financial Officer

**David Clark, M.D.**  
Chief Medical Officer

**David McMullin, M.B.A.**  
Chief Commercial Officer

**Stephen Machatha, Ph.D.**  
SVP Technical Operations



## Board of Directors

**Richard Douglas, Ph.D.**  
CHAIRMAN

**Ben Bronstein, M.D.**

**Marty Joyce, M.B.A.**

**Nancy Miller-Rich**

**Gary Phillips, M.D.**

**Jesse Treu, Ph.D.**

**Neal Walker, D.O.**

**Todd Brady, M.D., Ph.D.**

Former SVP Corporate Development at Genzyme

Former CEO Peptimmune<sup>8</sup>

Former CFO of Serono USA

CEO M-R Associates

CEO OrphoMed

Domain Associates

CEO Aclaris Therapeutics

CEO Aldeyra Therapeutics

1. Acquired by Xanthus/Antisoma  
2. Acquired by Schwarz/UCB  
3. Acquired by Alexion  
4. Acquired by Takeda

5. Acquired by Ligand  
6. Acquired by Merck  
7. Acquired by Alexion  
8. Acquired by Genzyme





# A New Paradigm for the Treatment of Immune- Mediated Diseases